had received 3 or more treatment regimens. Prior therapy included R in half of all patients. 12 patients had never achieved a complete remission, and 8 had primary refractory disease. Toxicity was similar to that reported with BEAM alone and included a fall in DLCO for most patients with 1 patient experiencing a transient decline to below 50% of the predicted values corrected for hemoglobin. Grade III/IV toxicities included infection, fever, stomatitis, nausea, vomiting, diarrhea, hemorrhage, and edema. One patient at the 700 cGy level developed veno-occlusive disease which constituted a dose-limiting toxicity (maximum total bilirubin 10.4), necessitating the enrollment of 3 additional patients at that dose level. Ascites resolved by D +34, and total bilirubin was normal by D +60. At the 700 cGy level, administered radioactivities ranged from 0.27 to 0.73 mCi/kg (median: 0.37), and the total body dose from 43 to 12 cGy (median: 99 cGy). In all but one case, the critical organ was the liver. Engraftment by ABMTR criteria occurred at a median of 10 days (range: 8-18) for 1000 granulocytes and 21 days (range: 12-40) for platelet recovery to 20,000. With a median follow-up of 12 months, the OS is 60% at 3 years. PFS is 47% at both 2 and 3 years. Accrual continues at the 900 cGy dose level which is anticipated to require greater than the .4 mCi/kg dose of $^{90}$ Y Zevalin recommended for conventional treatment.

## PEDIATRIC DISORDERS

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### A DECADE OF MYELOABLATIVE HLA-MATCHED SIBLING MARROW TRANSPLANTATION FOR CHILDREN WITH SEVERE SICKLE CELL DISEASE: OUTCOMES AND LESSONS LEARNED FROM THE ATLANTA EXPERIENCE

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Allogeneic BMT offers a cure to select patients with sickle cell disease (SCD), but the limited available long-term data and concerns about the risk-to-benefit ratio present dilemmas for families and clinicians. We report favorable outcomes in a large single institution experience with myeloablative matched sibling BMT for children with severe SCD between December 1993 and April 2003. Sixteen patients (12 male) with a median age 7.7 years (3.3-17.1) were transplanted for primary indications of CVA (n = 8), recurrent TIA (n = 1), recurrent ACS (n = 6), and frequent VOC pain (n = 1). Graft source was HLA-identical sibling marrow, with 9 HgbAS donors. Preparative regimen (BU 14 mg/kg, CTX 200 mg/kg, ATG 90 mg/kg) was well tolerated. Special measures included aggressive management of hypertension and hypomagnesemia, maintenance of Hgb 10-12 g/dl and platelets >50k, and prolonged antiepileptics while on CSA for GVHD prophylaxis. The initial 8 patients were treated on a multicenter consortium trial (Walters et al). With median follow-up 36 months (6-84), OS and DFS are 100% and there are no graft failures. Two patients have stable mixed chimerism (72 and 69% donor) with low HgbS (0 and 2.5%) and no clinical SCD. Median WBC engraftment was day 12.5 (10-21) and platelet engraftment day 31.5 (17-46). No patients experienced aGVHD. The two oldest patients had cGVHD related to medication non-compliance. Two of the 8 patients with prior CVA had serious CNS events, including seizure and hemorrhage on day 0 in a moya-moya patient and late progressive cerebrovascular disease in a patient with prior CVA. None had new clinical CVA. One patient (age 16.7 years) without prior CVA had a seizure attributed to "non-compliance rebound" with CSA. Infections included two episodes of Zoster, one early multiorganism bacteremia, and one late pneumococcal bacteremia. All patients have excellent functional status and attend school/college. These favorable outcomes have led our center to offer this transplant treatment as a standard-of-care with principles specific to SCD: 1)careful psychosocial screening and transplantation at a young age, 2)supportive measures to avoid CNS events, and 3) long-term follow-up with attention to infection and cerebrovascular disease that may relate to SCD rather than the BMT. In our experience, collaborative management with a comprehensive sickle cell program optimizes referral of appropriate patients, reduces peritransplant complications, and optimizes outcomes.

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### BONE MARROW TRANSPLANTATION (BMT) FOR CHILDREN AND ADOLESCENTS WITH SEVERE ACQUIRED APLASTIC ANEMIA (SAA): A SINGLE CENTER EXPERIENCE IN 171 PATIENTS (PTS) COMPARING TWO DIFFERENT PREPARATORY REGIMENS

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**Background:** BMT from a histocompatible sibling is the treatment of choice for young pts with SAA. Those who have received few transfusions can achieve long term survival after conditioning with Cyclophosphamide 200mg/kg (CY200). For pts heavily transfused, graft failure (GF) after this regimen is high and led to the addition of Anti-lymphocyte globulin to improve outcome. Unfortunately this drug is not easily available in developing countries and from 01/03 on, all pts with more than 15 transfusions pre-BMT were given Busulfan 12mg/kg (BU12) and CY 120mg/kg (CY120). **Material and Methods:** Between 10/79 and 09/03,396 pts with SAA were transplanted at our BMT Unit. In this study we performed a retrospective analysis in 171 pts <21 years, who received an HLA-identical sibling transplant (bone marrow), and methotrexate + cyclosporine as GVHD immuneprophylaxis. All pts received prophylactic antibiotics according to common practice. Preparatory regimen: CY200: 92 pts and BU12/CY120: 79 pts. Median age at transplant: 13yr (range 1 – 20yr). Gender: 64F/107M. Median disease duration: 3m (range: 0-232m). Median transfusions pre-BMT: 23UI (range: 0-238). TNC: 1, 48–12, 9 × $10^8$/kg (M: 3, 36). **Results:** 122 pts are alive and well 263-6141 days post-BMT (M: 2664 days). In the CY200 group 40 pts received >15 transfusions and 34 were evaluable for engraftment: 2 pts had primary GF and 20 had late GF (Median: 288 days; range: 100-734 days post-BMT). Mucosytis occurred in 9/92pts. A-GVHD grade III-IV occurred in 3/84 evaluable pts and extensive C-GVHD in 2/78pts. Estimated overall survival in 16 years is 86% for pts <15 transfusions and 50% for pts >15 transfusions. In the BU12/CY120 group, 76 pts were evaluable for engraftment, 1 pt had primary GF and 11 had late GF (median: 524 days post-BMT). Mucosytis grade III-IV occurred in 27 pts. 8/76pts had A-GVHD grade III-IV and 8/72pts had extensive C-GVHD. Estimated overall survival in this group is 70% (P value = 0.002). Forty-nine pts are dead: Bu12/CY120: 22 pts, CY200 > 15: 20pts and CY200 < 15: 7 pts). .Causes of death in both groups were mainly related to infection. **Conclusion:** The BU12 + CY120 regimen decreased the GF rate and improved overall survival for pts heavily transfused but it was associated with more toxicity and higher transplant related mortality.

## SOLID TUMORS

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### LESSONS FROM A POSITIVE RANDOMIZED TRIAL OF HIGH-DOSE CHEMOTHERAPY IN METASTATIC BREAST CANCER: LEARN FROM OUR MISTAKES, BUILD ON OUR SUCCESSES, DRAIN THE BATHWATER, HOLD THE BABY

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